Bitzur R. Phytosterols: another way to reduce LDL cholesterol levels

International Heart and Vascular Disease Journal. 2013; 1: 25-30

Summary

Phytosterols are sterols found naturally in various oils from plants. Phytosterols compete with cholesterol for a place in the mixed micelles, needed for cholesterol absorption by the small intestine. As a result, cholesterol absorption, either from food or from bile salts is lowered by about 50%, leading to a lowering of about 10% of blood cholesterol level, despite an increase in hepatic cholesterol synthesis. This reduction is achieved when phytosterols are given both as monotherapy, and in addition to statin therapy. The average Western diet contains about 400–800 mg of phytosterols per day, while the dose needed for lowering the blood cholesterol level is about 2–3 grams per day. Therefore, for the purpose of reducing blood cholesterol, they should be given either as phy-tosterol-enriched food or as supplements. The reduction in the level of low-density lipoprotein (LDL) cholesterol achieved with phytosterols may reduce the risk of coronary disease by about 25%. For this reason the American Heart Association has recommended the consumption of phytosterols, as part of a balanced diet, for lowering blood cholesterol levels.

High levels of LDL cholesterol is a well known risk factor for atherosclerosis, which is the main cause of mortality in Western countries [1]. Statins are the drugs of choice for people who are at high risk of developing cardiovas-cular diseases, and who have LDL cholesterol levels higher than recommended [2]. Following recent studies, low LDL cholesterol target levels have been set for high-risk patients. Such target levels mandate the use of high doses of potent statins in many cases [2]. Some of these high-risk patients fail to reach LDL cholesterol target levels even with intensive statin therapy. Moreover, 10–20% of statin-treated patients develop side effects (mainly myopathy), which limit the ability to use intensive statin therapy [3]. Potential therapies in such cases include ezetimibe, bile acid sequestrants and niacin [2]. Another treatment option which gathered renewed interest in re-cent years is the use of phytosterols. Phytosterols are plant-derives sterols that inhibit the intestinal absorption of cholesterol. This review covers current knowledge on cholesterol absorption and the available data concerning phytosterols efficacy and safety.

Keywords

Phytosterols, sterols, stanols, cholesterol

**Zlatohlavek L. Statin myopathy as a clinical problem. Can we help?**

International Heart and Vascular Disease Journal. 2014; 3: 30-35

**Abstract**

**Objectives.** Statins reduce low density lipoprotein (LDL) cholesterol and prevalence of atherosclerosis. Unfortunately, as statins also have side effects, e.g. dyspepsia, hair loss, insomnia and statin- myopathy, some statins cannot be administered in sufficient doses or administered at all. The aim of this study was to demonstrate the effect of coenzyme Q10 in patients with statin myopathy.

**Design/setting.** The aim of our study was to show the effect of administration of coenzyme Q10 (CoQ10) by statin myopathy. 28 patients (18 women and 10 men) aged 60.6±10.7 years were observed. Muscle weakness and pain was monitored. Pursuance of muscle pain and weakness were performed prior to administration of CoQ10 and after 3 and 6 months of dosing. Statistical analysis was performed using Friedman test, Annova and Students t-test.

**Results and conclusion.** Pain decreased on average by 53.8% (P<0.0001), muscle weakness by 44.4% (P<0.0001). After administration of CoQ10 over 6 months, muscle pain and sensitivity significantly decreased.

**Key words**

Statin, side effect, statin-myopathy, coenzyme Q10

**Acknowledgement**

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**Tabl M.A., Attia A.I., Hamouda M.A., Farag E., Mansour H.A. High-density lipoprotein cholesterol as a predictor of clinical outcomes in patients achieving low lipoprotein cholesterol targets after elective percutaneous coronary intervention**

International Heart and Vascular Disease Journal. 2015; 6:26-32

**Abstract**

**Objective.** To investigate the significance of high-density lipoprotein (HDL) cholesterol after statin therapy on the outcomes of patients with coronary artery disease (CAD) who underwent elective percutaneous coronary intervention (PCI).

**Materials and methods.** One hundred patients with CAD were included in this prospective study. All patients had elective PCI with their baseline LDL cholesterol less than 100 mg/dL. Patients were classified according to baseline HDL cholesterol into two groups: group I with normal HDL cholesterol levels (> 40 mg/dL for men or >50 mg/dL for women) and group II with low HDL cholesterol levels. Major adverse cardiac events (MACE) were reported in both groups at 6-month follow-up.

**Results.** During the follow-up, the low HDL cholesterol group had insignificantly higher rates of composite MACE. HDL cho-lesterol levels were inversely related to the occurrence of composite MACE (odds ratio for MACE: 0.3697, 95 % CI: 0.1421 to 0.9619; P=0.0414). Low HDL cholesterol on follow-up was a significant predictor of target vessel revas-cularization (TVR) (P=0.009).

**Conclusion.** Low HDL cholesterol was associated with high MACE after elective PCI and thus clearly influenced the prognosis.

**Keywords**

Coronary intervention, high-density lipoprotein, low-density lipoprotein

**Nevrez Koylan, Mamedov M.N.**

**Opportunities of new lipid-lowering therapy: proprotein convertase subtilisin/kexin type 9 inhibitors’ clinical efficacy and safety profile**

International Heart and Vascular Disease Journal. 2016; 11: 3-7

**Summary**

Safe and evident reduction of LDL cholesterol in order to reduce the risk of cardiovascular complications is animportant problem of modern cardiology. Results of new clinical placebo-controlled comparative studies investigating proprotein convertase subtilisin/kexin type 9 inhibition with monoclonal antibodies (mAb) indicate highpotential of new group of drugs. This review article analyzes clinical efficacy and safety profile of alirocumab andevolocumab as a part of combined statin therapy.

**Keywords**

Lipid-lowering therapy, proprotein convertase subtilisin/kexin type 9 inhibitors

# **Klimushina M.V., Gumanova N.G., Gorshkov A.Y., Gavrilova N.E., Metelskaya V.A. Interrelation between statins and endothelial dysfunction marker in male and female patients with coronary atherosclerosis**

# International Heart and Vascular Disease Journal. 2016; 11: 27-31

# **Summary**

**Objective.** To analyze the interrelation between the marker of endothelial dysfunction endothelin and hypolipedemic drugs administration in patients with verified coronary arteries (CA) lesions

**Materials and methods.** This study included 429 patients (302 males and 127 females) in the age of 62,7±8,8 years with CA lesions verified with coronary angiography. Endothelin levels in serum were measured with immune-enzyme assay ELISA.

**Results.** Negative correlation between statins therapy and endothelin levels was identified in male patients(r= -0.11, P=0.04).We revealed that males undergoing statin therapy (n=294) had 1,8 times less endothelin levels comparingwith the men who did not receive statins. The interrelation between statin administration and endothelin levels infemale patients with CA lesions was not found.

**Conclusion.** In male patients with CA lesions, as opposed to females, statin administration correlates negatively with endothe-lin levels and is associated with its 2-fold decrease. Interrelation between endothelin concentration and administration of other drugs was not found.

**Keywords**

Atherosclerosis, endothelial dysfunction, endothelin, statins

**Titov V.N. Common etiology, different pathogenesis and basics of atherosclerosis and atheromatosis prevention. Marked differences in lipoprotein-mediated fatty acids transport in blood of herbivores and carnivores.**

International Heart and Vascular Disease Journal. 2016; 12: 22-35

**Summary**

According to the phylogenetic theory of general pathology, increased consumption of meat by herbivorous animalsalways leads to the development of atherosclerosis and arterial intima atheromatosis. The following etiologicalfactors of atherosclerosis and atheromatosis have been developed during phylogenesis: a) cellular uptake of fattyacids (FA) with ApoВ-100 low density lipoproteins; b) human cells do not convert exogenous palmitic saturatedFA (SFA) into oleic monounsaturated FA (MFA), instead in vivo they enter non-physiological palmitic pathway ofFA metabolism and c) phylogenetically late monocytes→macrophages hydrolyze with low efficiency polyenic FAesterified with cholesterol (CL). Environmental influence, impaired biological function of trophology (nutrition)and impaired biological reaction of food consumption, including non-physiologically high content of palmitic SFAand CL in diet, are pathogenic factors of atherosclerosis and atheromatosis. Formation of circulating ligandlesspalmitic very low density lipoproteins (VLDL) is the key step of atherosclerosis and atheromatiosis pathogen-esis. Several problems arise under these conditions: a) how to utilize in vivo big amount of ligandless palmiticVLDL which affect the biological function of endoecology and the biological reaction of inflammation, thus creatingpathogenetic basis for atheromatosis and b) how can cells maintain their function if it is impossible to uptake polyenic FA from the extracellular medium, which creates the basis for atherosclerosis, impairs biological functionof adaptation and biological reaction of compensation. Physiological diet of Homo Sapiens consists mostly from carbohydrates, palmitic SFA synthesized de novo from glucose, insulin converts it to oleic acid that subsequentlyundergoes highly effective oxidation in mitochondria. At low dietary content of palmitic FA insulin promotes anoptimal oleic pathway of FA metabolism providing high “kinetic parameters” of the organism and efficient ATPproduction. According with common pathogenesis of atherosclerosis and atheromatosis, it is necessary to preventthe formation of ligandless palmitic VLDL. Their absence will make impossible the development of atherosclerosis and atheromatosis.

**Keywords**

Fatty acids, cholesterol, atherosclerosis, atheromatosis, biological function of endoecology

**Ralnikova N.A., Kalev O.F.**

**Lipid metabolism characteristics in women of childbearing age with iron-deficiency anemia.**

International Heart and Vascular Disease Journal. 2017; 14: 23-28

**Summary**

**Objective.** To determine interrelation between lipid metabolism characteristics with iron-deficiency anemia and other car-diovascular risk factors in women of child-bearing age.

**Materials and methods.** Using the results of complex population study of rural dwellers, we performed analysis of lipid metabolism char-acteristics and other cardiovascular risk factors in 506 women of child-bearing age.

**Results.** Women with iron-deficiency anemia (n=26) had significantly lower levels of total cholesterol (p=0,009), low den-sity lipoproteins cholesterol (p=0,003) and significantly lower atherogenic index (p=0,003). Regression analysisdemonstrated that the presence of iron-deficiency anemia is an independent factor that significantly reduces thepossibility to have atherogenic dyslipidemia in females of studied population (OR=0,20, 95% CI 0,07-0,55, p=0,002).

**Conclusion.** It is recommended to take into account the presence of iron-deficiency anemia in case of investigation of lipidmetabolism characteristics in women of child-bearing age.

**Key words**

Iron-deficiency anemia, hemoglobin, dyslipidemia, cholesterol

**Titov V.N., Rozhkova Т.А., Kaminnaya V.I. Phylogenetic theory of general pathology. Atherosclerosis and atheromatosis as two different processes: aphysiological implementation of biological function of trophology and endoecology.** International Heart and Vascular Disease Journal. 2017; 15:31-43

**Summary**

We believe that seven biological functions have formed during phylogenesis. They are: 1) trophology, 2) homeostasis, 3) endoecology, 4) adaptation, 5) reproduction, 6) locomotion, 7) cognitive function, including intellect. The function of trophology (feeding) is realized via the biological reaction of exotrophy (external feeding) and endotrophy (internal feeding). The function of endoecology provides the maintenance of all vital parameters within physiological range. This function is realized through the reactions of inflammation and excretion. Etiological factors of atherosclerosis are: 1) oleic monounsaturated fatty acid (MFA) that is more actively utilized in biochemi- cal reactions than palmitic fatty acid, 2) in the ocean all animals were carnivorous (fish eating), after millions of years of living on dry land Homo sapiens became herbivorous, 3)insulin plays the major role in transition from carnivorous to herbivorous belongs, since this hormone is involved in conversion of endogenous saturated pal- mitic (SFA) into oleic MFA, 4) phylogenetically insulin does not initiate in vivo conversion of exogenous palmitic SFA into oleic MFA, and 5) in the ocean, biologically active eicosanoids are synthesized from eicosapentaenoic polyenic FA (PFA); on dry land this acid is not available. Excessive eating of meat by herbivorous Homo sapiens provides the basis for atherosclerosis. Blocked bioavailability of PFA leads to their deficiency in cells. Insulin-initiated transport of oleic MFA as oleic triglycerides (TG) in oleic apoЕ/В-100 very low density lipoproteins (VLDL) occurs without LDL formation; transport of SFA in palmitic apoЕ/В-100 VLDL is blocked at the stage of nonligand palmitic VLDLLDL formation, glycolipoprotein formation and high level of LDL-cholesterol. Incomplete utilization of pal- mitic VLDLLDL by monocytes leads to atheromatosis in the intima of elastic arteries. Polyenic FA metabolites which were not internalized via apoB-100 endocytosis are the major constituents of atheromas. Atherosclerosis, hyperlipoproteinemia and high content of LDL-cholesterol result from impaired function of trophology, while ath- eromatosis is associated with impaired biological function of endoecology.

**Key words**

Atherosclerosis, atheromatosis, insulin, biological functions, LDL-cholesterol, arterial intima

**Samorukova E.I., Adasheva T.V., Zadionchenko V.S., Bagatyrova K.M., Li V.V.**

**Use of rosuvastatin in patients with chronic obstructive pulmonary disease.**

International Heart and Vascular Disease Journal. 2018; 17: 29-36

**Objective.** To investigate the effects of rosuvastatin on systemic inflammation, endothelial dysfunction, and clinical course of chronic obstructive pulmonary disease (COPD).

**Materials and methods.** This study included 110 patients with COPD and without history of cardiovascular events. These patients had high or very high cardiovascular (CV) risk (10.0 [8.0; 18.0]) according with the SCORE (Systematic Coronary Risk Estimation) scale. In order to correct CV risk, 90 patients with COPD were prescribed with rosuvastatin (10 mg) and dose titration up to reaching target levels of low density lipoprotein cholesterol according to CV risk calculated within 1 year. Control group consisted of 20 patients with COPD. We estimated the levels of high sensitive C-reactive protein (hs-CRP), inflammatory (Tumor Necrosis Factor *a* (TNF-*a*), interleukin-8 (IL-8)) and anti-inflammatory cytokines (IL-4, IL-10) in blood serum, and Vascular Cell Adhesion Molecule type 1 (VCAM-1).

Clinical course of COPD was estimated according to the number of COPD exacerbations and St.George’s Respiratory questionnaire. Tolerance to physical exercise was determined using 6 minute walk test.

**Results.** Therapy of rosuvastatin led to significant reduction of hs-CRP levels (21.5 %, p=0.001), TNF-*a* (26.7 %; p=0.001), IL-8 (32.6 %; p=0.001), IL-4 (15.4 %; p=0.001), IL-10 (16.5 %; p=0.001), VCAM-1 (28.9 %, p=0.003); number of COPD exacerbations (25 %, p<0.001), severity of COPD symptoms according to St.George’s Respiratory questionnaire (19.9 %, p<0.001). The tolerance to physical exercise increased (13.2 %, p<0.001). The main group demonstrated increased tolerance to physical exercise (13.2 %, p<0.001). Plasma levels of TNF-*a* (19.3 %; p=0.001) and IL-4 (30 %; p=0.001) were increased in the control group together with 5 % reduction of distance in 6 minute walk test (19 meters; p=0.001).

**Conclusion.** Rosuvastatin has anti-inflammatory, endothelium-protective, and immune-modulatory effects, influences the key systemic processes of COPD and CV diseases formation, and it can also modify the clinical course of COPD (reducing the number of exacerbations and severity of symptoms, improving tolerance to physical exercise), in patients with COPD. It is recommended to calculate CV risk and perform its correction according with the common guidelines in all patients with COPD.

**Key words**

Rosuvastatin, statins, chronic obstructive pulmonary disease (COPD), systemic inflammation, COPD exacerbation, COPD symptoms.

**Chumakova G.A., Pokutnev A.P., Veselovskaya N.G., Bobrovskaya L.A.**

**Relationship between the degree of epicardial fat volume and severity of coronary atherosclerosis.**

International Heart and Vascular Disease Journal

Background. Obesity is associated with high level of cardiovascular morbidity and mortality. During the last years it has been clarified that high cardiovascular risk correlates not only with total volume of adipose tissue, but mostly with increased amount of visceral fat tissue. Epicardial fat tissue is the most studied local visceral fat depot and a potent source of pro-inflammatory, pro-atherogenic, and neurohumoral factors.

Objective. To investigate the relationship between the degree of epicardial fat volume and coronary atherosclerosis severity

Materials and methods. This study included 156 men with coronary heart disease (CHD) aged 53.2±7.6 years with obesity I –III grade, BMI 34.5±5.6 kg/m2. All patients underwent measurement of metabolic and additional cardiovascular risk factors and coronary angiography. Epicardial fat tissue thickness (EFT) was evaluated using transthoracic echocardiography.

Results. The highest values of EFT were observed in the group of patients with multiple stenosis of coronary arteries where EFT reached 10 (8; 10) mm. ROC-analysis revealed EFT as a predictor of significant coronary atherosclerosis in patients with CHD. Sensitivity and specificity of this marker were 80.4 % and 67.6 %, respectively (cut-off value=6 mm). It was found that EFT correlated significantly with the presence and severity of coronary atherosclerosis together with age, leptin and resistin levels, and waist circumference.

Conclusions. Our results prove the necessity of addition of obesity-correcting measures, targeting first of all visceral obesity, into programs of atherosclerosis prevention including coronary atherosclerosis.

Key words

Epicardialfat tissue, coronary atherosclerosis.

**Derbeneva S. A., Nesterova V. E., Zaletova T. S., Feofanova T. B.**

**New possibilities of dietary correction of residual lipid metabolism disorders in patients with coronary artery disease and obesity.**

International Journal of Heart and Vascular Diseases. 2020; 8 (27): 29-37

**Abstract**

**Aim.** To estimate the dynamics of lipid panel in patients with coronary artery disease (CAD), obesity and residual dyslipidemia, who receive optimal statin therapy and follow standard low-calorie diet with additional lipid-lowering product (LLP).

**Materials and methods.**

This study included 40 patients with severe coronary atherosclerosis manifestations, who were selected for surgical revascularization of myocardium due to multiple vascular lesions and / or stenosis of proximal segments of the coronary arteries and with non-target atherogenic lipoproteins levels during optimal statin therapy. We also estimated additional effect of standard low-calorie diet (LCD) and LLP on the lipid panel.

**Results.** The results showed that 30-days follow-up of LCD could significantly decrease total cholesterol (TC) level by 15,7 % (p = 0,0003) and low-density lipoproteins (LDL) by 19,1 % (p = 0,0024), and the additional intake of LLP increased the efficiency of LCD and contributed to the achievement of reliable reduction of TC by 32.9 % (p < 0.0001), LDL by 38.1 % (p < 0.0001), very low density lipoproteins (VLDL) by 44, 5 % (p =  0.013) and atherogenic coefficient of 35.2 % (p =  0.003).

**Conclusion.** Based on the obtained results we can conclude that low-calorie diet for the correction of residual dyslipidemia during the standard statin therapy was superior to statin therapy potentiation and was associated with lower drug-loading.

**Key words**

**C**oronary artery disease, lipid metabolism, diet, obesity.